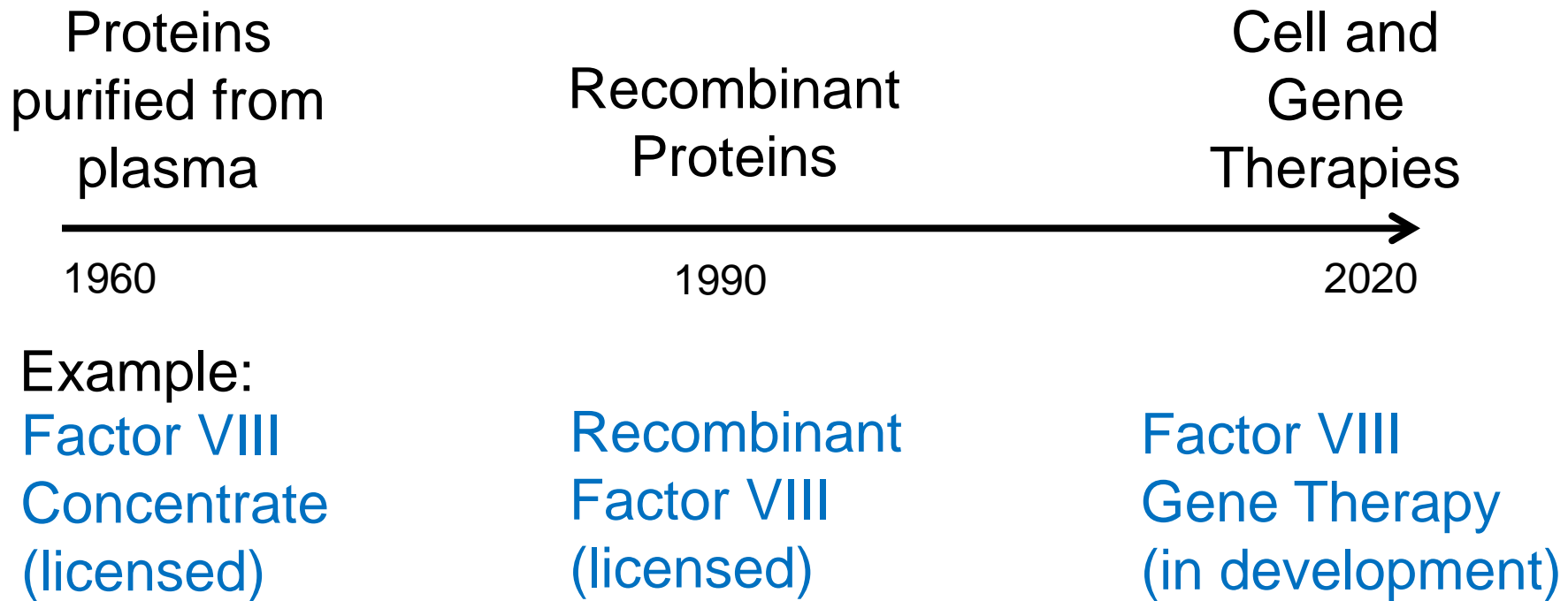


Gene Editing: CBER's Perspective

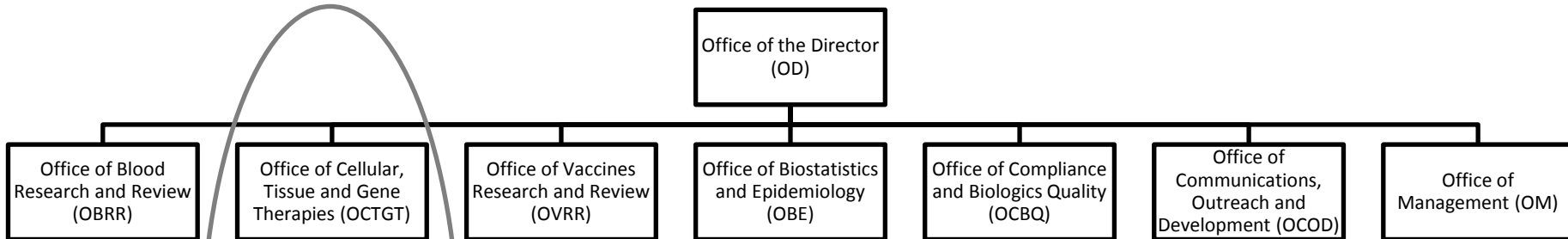


FDA Science Board Meeting
November 15, 2016

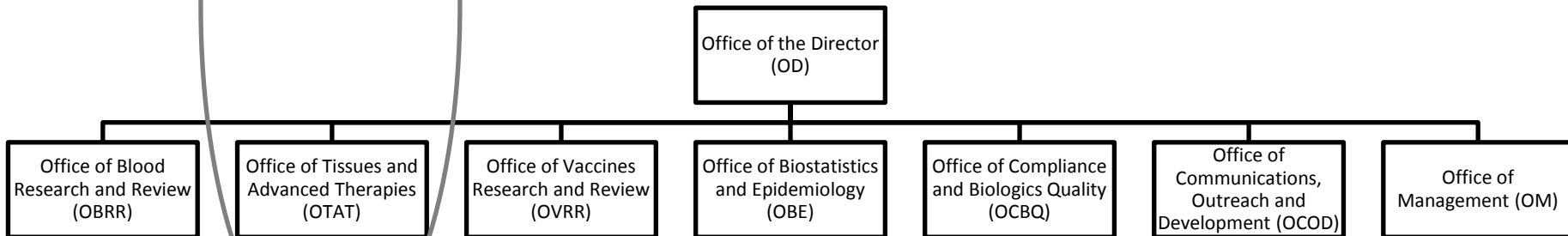
Evolution of CBER's Products



Prior to Reorganization



Following Reorganization



Effective Date: October 16, 2016



Preparing for the Future at CBER

- Three new PI's recruited to address emerging scientific needs relevant to our regulated products, including gene editing, gene-modified T cells, and tissue engineering
- Participation in public meetings and workshops on gene editing
- Participation in the Recombinant DNA Advisory Committee Process with NIH
 - Non-voting member

Continued FDA Education





**U.S. FOOD & DRUG
ADMINISTRATION**

FDA and Health Research Alliance present:
Gene Editing Workshop: Technologies and Applications on FDA-Regulated Products

November 1, 2016
8:00 am - 5:00 pm
 WO Bldg 31 Great Room

Keynote Speaker:
Jennifer Doudna, PhD
*HHMI Investigator,
 Howard Hughes Medical Institute,
 Innovative Genomics Initiative,
 University of California*

Session Speakers:

J. Keith Joung, MD, PhD
*Associate Chief of Pathology for Research,
 Professor, Massachusetts General Hospital and
 Harvard Medical School*

Matthew Porteus, MD, PhD
*Associate Professor, Pediatrics
 Stanford University, School of Medicine*

Joseph Tector, MD, PhD, FACS
*Professor of Surgery
 University of Alabama at Birmingham*

Paul A. Nakata, PhD
*Molecular Biologist, Assistant Professor
 Children's Nutrition Research Center*

Silvana Konermann, PhD
Researcher, Salk Institute for Biological Studies

Contact: Devin.Thomas@fda.hhs.gov www.fda.gov



FDA Co-Sponsored Study

- National Academies of Sciences, Engineering, and Medicine Consensus Study on human gene editing: scientific, medical, and ethical considerations
- Will provide a framework based on fundamental, underlying principles that may be adapted and adopted by any nation that is considering the development of guidelines

Gene Editing Technology

- DNA inserted, deleted, or replaced in the genome of an organism using engineered nucleases (“molecular scissors”)
- Nucleases create site-specific double strand breaks (DSBs) at desired locations in the genome and the breaks are repaired through non-homologous end-joining (NHEJ) or homology directed repair (HDR) resulting in targeted mutations (edits)

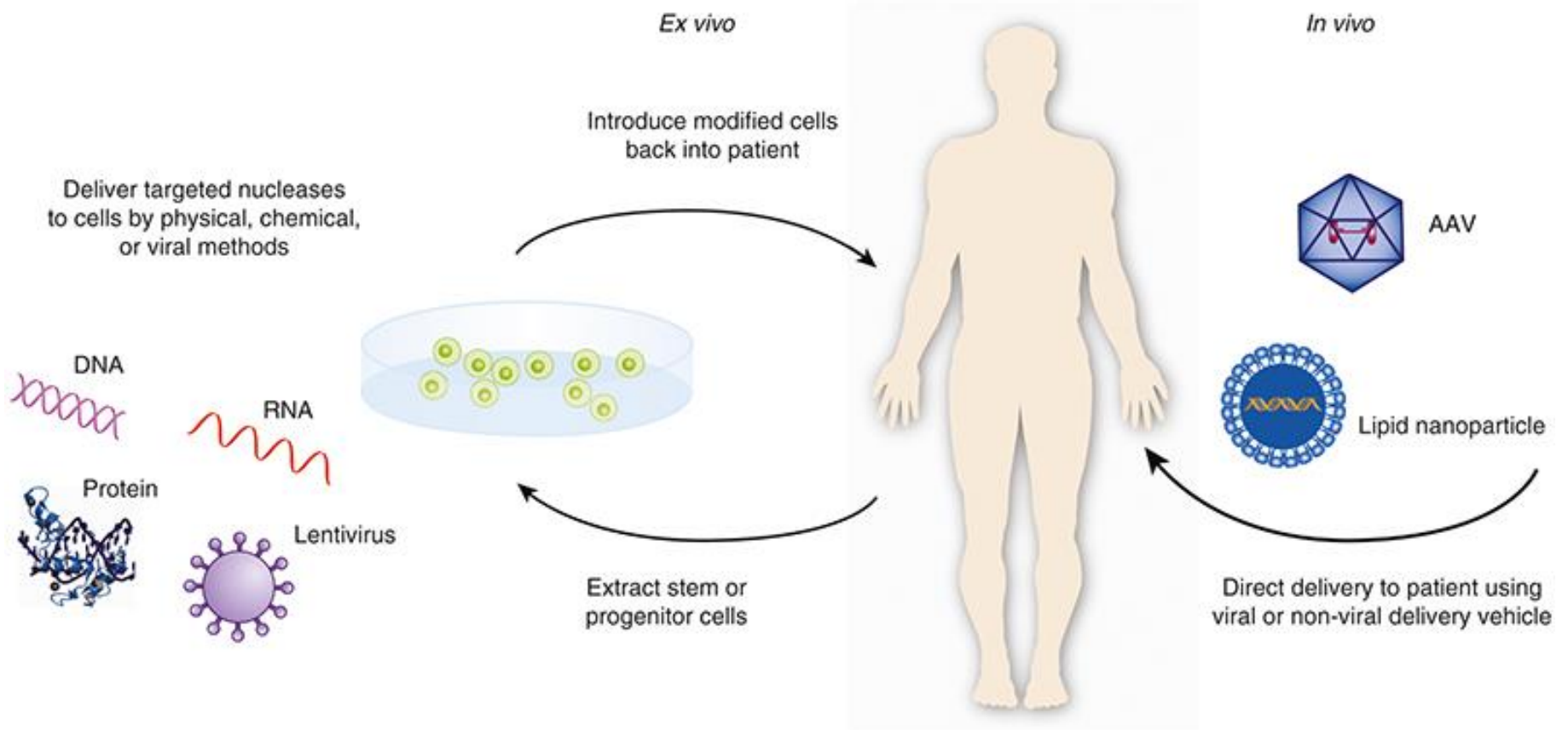
Nucleases for Gene Editing

- Zinc Finger Nucleases (ZFNs)
- Transcription Activator-Like Effector Nucleases (TALENs)
- Engineered Meganucleases
- Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR/Cas9)

Potential for Gene Editing

- Possible to modify somatic cell or germline genomes through relatively efficient targeted genetic modification, inactivating, inserting or changing genes
- FDA regulates somatic and germline gene modifications used as therapeutics in humans
 - Includes modification of cells prior to administration and gene therapy vectors
 - Somatic cell versus germline editing is currently relevant in humans

Ex vivo or In vivo Gene Editing



Scientific Considerations

Desirable

- Efficient delivery
- On target gene modification
- Targeted expression
- Long lasting expression
 - Depends on indication

Undesirable

- Immune response to vector or transgene
- Off target editing
- Off target expression
- Insertional mutagenesis

Other Considerations

- Potential germline transmission

Regulatory Considerations

- Nature of editing
 - Inactivation, insertion, modification
- Safety considerations
 - Percentage of cleavage at on- and off-target sites
 - Evaluation of the profile of insertions and deletions and types of mutations generated
- Science-based approach to regulation
- Benefit-risk analysis

